





April 18, 1978

CONFIDENTIAL

E21

## Anti-dandruff activity of Octopirox

( = H 72 6146 A = ASM-D)

Octopirox (=monoethanolamine salt of the 1-hydroxy-4-methyl-6-(2,4,4-trimethylpentyl)-2-pyridone) was tested for its anti-dandruff activity in eight test series between 1972 and 1978. A total of 168 test persons received Octopirox in shampoo bases ineffective against dandruff on one side of the head and, in comparison, the established anti-dandruff agents zinc or zirconium-Omadine<sup>R</sup> (zinc or zirconium salt of the pyridinthione-N-oxide) on the other side of the head. The studies were performed by the Hans Schwarzkopf GmbH, Hamburg, in co-operation with Prof. Dr. Michael Jänner of the university dermatological and policlinic in Hamburg-Eppendorf (director : Prof. Dr Dr J. Kimmig). In the established method (cf. Appendix 1) employed in these studies, Octopirox showed an equally good anti-dandruff activity as the above reference compounds. A critical evaluation of the results of the individual test series even shows advantages of Octopirox in several respects.

The enclosed Appendices 2 - 5 are typical examples of reports and expert opinions confirming the anti-dandruff activity of Octopirox.

signed:

Appendices

Dr Futterer

## A P P E N D I X 1

Hamburg, February 15, 1971

Copy of instructions by the Hans Schwarzkopf GmbH

### Testing and treatment method for the examination of anti-dandruff agents

#### 1.1 Selection of models

Test persons with medium-grade to marked dandruff were selected for the study. Attention was paid to the fact that only test persons with a uniform intensity dandruff which affected the entire head were chosen. The test persons were selected in the presence of a dermatologist. Test persons with scalp diseases were not accepted.

#### 1.2 Instructions for test persons

The test persons had to affirm that for eight weeks they would not use any shampoos or hair cosmetics other than those given to them by hair-dressers conducting the tests. This means that the test persons were not allowed to wash their hair themselves, they were allowed to use hair spray only according to instructions by the hair dressers, and that they had to follow the hair-dressers' instructions in general.

#### 1.3 Assessment

The condition of the scalps was assessed prior to each hair-wash

by four assessors independent of each other. The results of assessment were given in four grades:

3 = marked dandruff

2 = medium-grade dandruff

1 = dandruff no longer detectable for test persons.

The tester finds isolated dandruff.

0 = completely free from dandruff

This grading proved to be appropriate, as it corresponded approximately to the percental relationship, i.e. 1 corresponds to approximately one third of the dandruff amount of 3, etc.

#### 1.4 Course of study

After the selection of test persons and the assessment of initial values, one of the test hair-dressers parted the hair of the test persons in the middle, and then the hair was washed unilaterally with shampoo A or B.

Prior to shampooing each side of the head was wetted evenly, followed by the unilateral hair wash (first wash). After an even rinsing of both sides of the head the main hair wash was performed. During these procedures the principle of identical treatment of each side of the head (time for shampoo to take action, amount of rinsing liquid, temperature of rinsing liquid, etc.) was strictly followed. After drying the hair of each side of the head was set without any follow-up treatment. In women, setting lotion was subsequently applied onto the rollers.

The hair thus was dried under a drying hood at a temperature of up to a maximum of 50° C. Subsequently the hair was styled.

The unilateral hair washes etc. were repeated twice a week during the first weeks of the study and once each during the following four weeks. The four assessors always examined the condition of the hair prior to each hair wash.

Fourteen days after the last treatment the entire head was washed with the drug-free shampoo. If the hair needed washing in the meantime, it was also washed with a drugfree shampoo.

After another two weeks the final assessment was performed.

#### 1.5 Evaluation

Each assessor submitted the values he had obtained, and then the mean values of the 'dandruff value' of each test person were added and divided by the number of test persons. The mean value thus obtained was plotted in a curve. The points were converted into per cent figures. Thus, three points represented 100 per cent, 2 points represented 66 per cent, i.e. if the test series is started with 50 per cent of the test persons with a grading of 2 points and 50 per cent with the grading 3 points, a starting point of approximately 83 per cent is obtained.

## A P P E N D I X 2

Hamburg, December 14, 1974

Copy of the Report by the Hans Schwarzkopf GmbH

### Anti-dandruff test series 360/73

In 29 test persons unilateral hair washes were performed with shampoos Nos. 54 and 56.

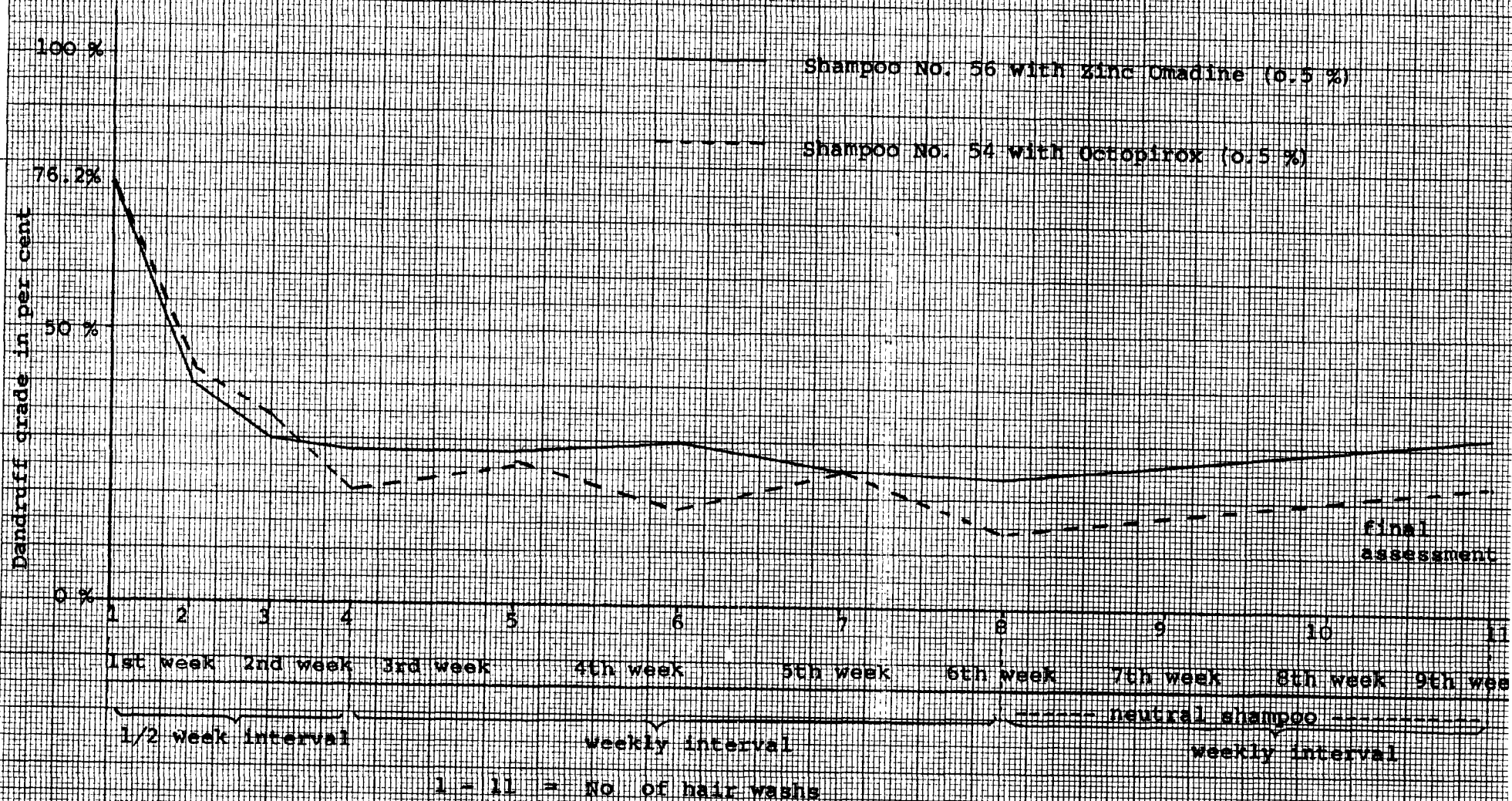
At least four assessors examined the condition of the hair up to the 8th treatment. After three hair washes with neutral shampoos the condition of the hair was finally assessed in the presence of Prof. Jänner.

Two test persons dropped out of the test because of illness, one further test person was excluded from the study when a psoriasis was diagnosed. Thus, the values obtained from 26 test persons were evaluated. The results are illustrated in the enclosed Figure.

No. 56 = anti-dandruff shampoo + 0.5 per cent Zn-Omadine<sup>®</sup>

No. 54 = anti-dandruff shampoo + 0.5 per cent ASM-D (Octopirox)

Figure to Appendix 2:



### A P P E N D I X 3

Hamburg, May 23, 1974

Copy of an expertise from the University Dermatological Hospital,  
Hamburg

The following dermatological expertise refers to the clinical efficacy of the anti-dandruff test shampoo No. 54 and the anti-dandruff test shampoo No. 56 in the normal (seborrhoeic) dandruff formation.

#### Purpose

The purpose of this study was to clarify to what extent the above compounds are suitable for the cure of normal (seborrhoeic) dandruff formation and whether there is a difference in efficacy between these two compounds.

#### Method

The studies were performed according to an established and appropriate method already described in previous expertises.

At the beginning of the study, patients whose dandruff formation was due to pathological changes of the skin of the head were rejected.

The evaluation of the effect was, as before, graded with one to three crosses ( + to +++ ) according to degree of dandruff formation. Hair



which was completely free from dandruff was given a negative grade (Ø). The meaning of these symbols has already been described in previous expertises so that a further description does not seem necessary. The same applies to the description of the course of the study.

The hair of 26 test persons was examined. Initial findings and final results are given in the enclosed Table.

### Results

Prior to the beginning of the study, eight of the 26 test persons treated with the test compound No. 54 showed very marked dandruff formation which was marked +++. Eighteen test persons showed a medium-grade dandruff formation which was marked ++. After the conclusion of the consistent treatment, two test persons were completely free from dandruff, nine test persons showed dandruff in physiological quantities, in fourteen test persons the dandruff formation was still visible, and one person showed medium-grade dandruff formation. The latter, however, showed a certain positive effect of the compound, as the intensity of dandruff formation had decreased from +++ to ++. An absolute lack of efficacy was not observed in any of the test persons.

When adding the test persons free from dandruff and those with only slight dandruff at the end of the treatment, a total of 42.30 per cent of test persons showed a satisfactory, the rest an unsatisfactory decrease of seborrhoeic dandruff formation on their scalps.

Ø	7,69 %	+	53,84 %
(+)	34,61 %	++	3,84 %
	42,30 %		57,68 %
satisfactory improvement		unsatisfactory improvement	

The 26 test persons treated with test compound No. 56 of course showed the same degree of dandruff formation prior to the beginning of treatment, as they were the same test persons and were treated according to the same method.

After conclusion of treatment no test person was completely free from dandruff, eleven test persons showed dandruff in physiological quantities. This degree of dandruff formation was marked (+). In 13 test persons a clearly visible dandruff formation was found which corresponded to the grade +. In two test persons a medium-grade dandruff formation was observed.

Ø	-
(+)	42,30 %
	<hr/>
	42,30 %

satisfactory improvement

+	50,-- %
++	7,69 %
	<hr/>
	57,69 %

unsatisfactory improvement

When comparing the two test compounds used in this study, and when regarding the findings Ø (free from dandruff) and (+) (Physiological quantity) as a satisfactory improvement and the findings + (clearly visible dandruff formation) and ++ (medium-grade dandruff formation) as unsatisfactory improvement, there is no difference between the effects of the two test compounds.

The local tolerance of compounds No. 54 and 56 was good.

signed:

Prof. Jänner

#### A P P E N D I X 4

Hamburg, April 30, 1974

Excerpt from the report of Hans Schwarzkopf GmbH

Dandruff test with the active substance Zinc Omadine® in comparison  
with Octopirox ( H 72 6146 A, former name ASM-D)

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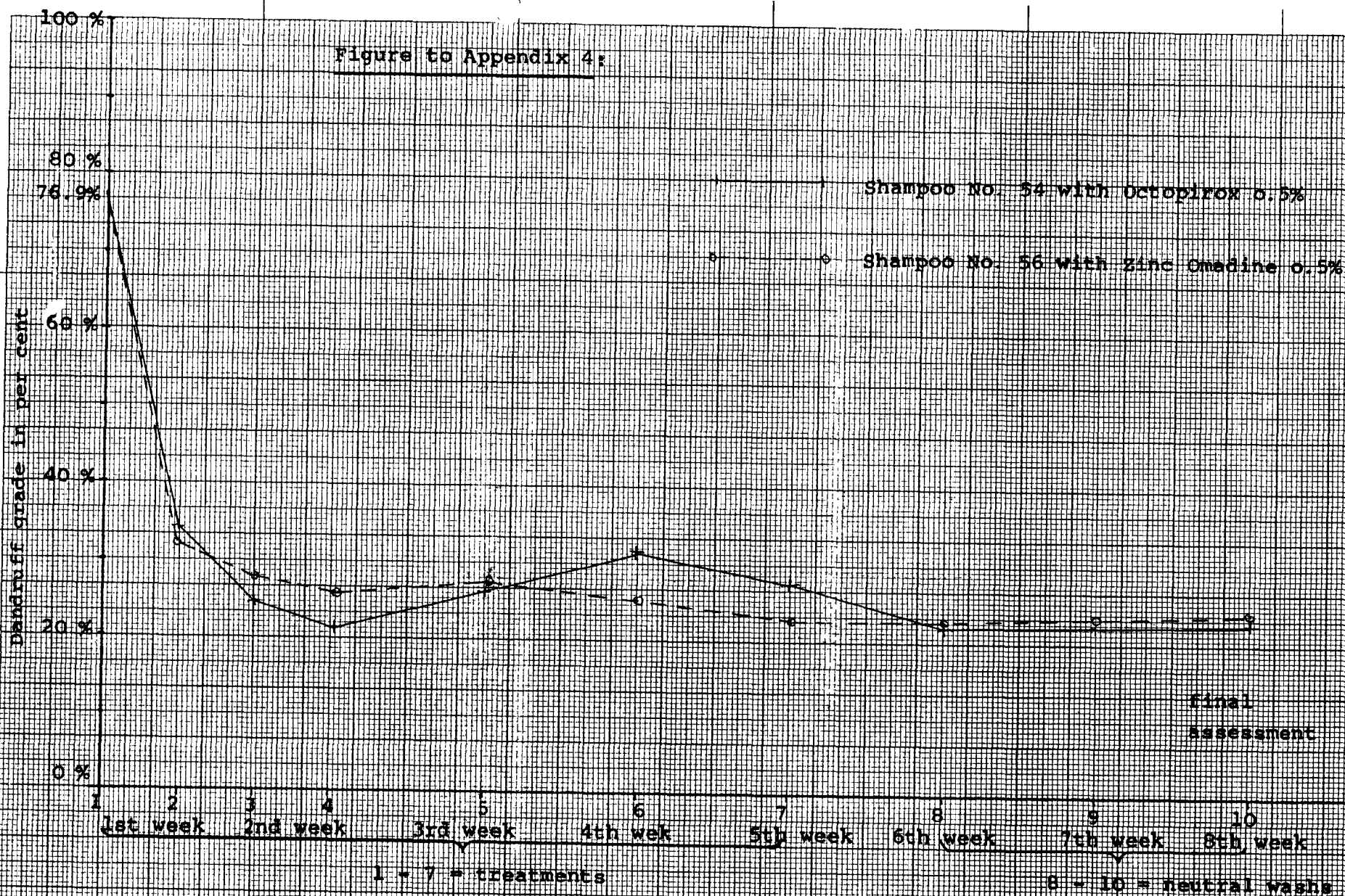
The shampoo base corresponded to the commercial product 'Seborin Antidandruff Shampoo, mfr.: Hans Schwarzkopf GmbH. The attached Figure shows the results of the 10-week test in 27 test persons. After ten weeks of treatment the initial value of approximately 77 per cent dandruff formation had decreased to approximately 22 per cent after treatment with Octopirox and approximately 24 per cent after treatment with zinc Omadine®.

Compound No. 56 = Seborin shampoo base + 0.5 per cent Zn-Omadine

Compound No. 54 = Seborin shampoo base + 0.5 per cent Octopirox

Din A 4 210 x 297 mm

Figure to Appendix 4:



## A P P E N D I X 5

Hamburg, December 18, 1974

Copy of an expertise from the University Dermatological Hospital,  
Hamburg

The following dermatological expertise refers to the clinical efficacy of the anti-dandruff test shampoos No. 56 (new) and 54 in the normal (seborrhoeic) dandruff formation. This expertise is to state to what extent the above compounds are suitable for the cure of normal (seborrhoeic) dandruff formation and whether there is a difference in efficacy between these two compounds.

The studies were performed according to an established and appropriate method already described in previous expertises. At the beginning of the study, test persons whose dandruff formation was due to pathological changes of the skin of the head were rejected.

The effect of treatment was, as before, evaluated according to the degree of dandruff formation and was marked with symbols. These symbols were crosses and indicated the degree of dandruff formation, ranging from one to three crosses. Hair which was completely free from dandruff was given a negative grade ( $\emptyset$ ). The meaning of these symbols has already been described in previous expertises so that a further description does not seem necessary. The same applies to the description of the course of the study.

The effect of the compound was examined in thirty test persons. Initial findings and final results are given in the enclosed Table.

1 test person	Ø	3.33 %
13 test persons	(+)	43.33 %
13 test persons	+	43.33 %
3 test persons	++	10.00 %
<hr/>		
30 test persons		99.99 %

In each test person, one side of the scalp had been treated with test compound No. 54, and the other side of the head had been treated simultaneously and in the same way with test compound No. 56 new. The initial finding corresponds to that of previous studies. The normal (seborrhoeic) dandruff formation usually occurs fairly symmetrically.

After the conclusion of the active washs no test person was completely free from dandruff. Five test persons showed dandruff in physiological quantities, fifteen test persons showed visible dandruff formation, seven test persons showed a medium-grade dandruff formation, and in three test persons a very marked dandruff formation was observed.

no test person	Ø	
5 test persons	(+)	16.66 %
15 test persons	+	50.00 %
7 test persons	++	23.33 %
3 test persons	+++	10.00 %
<hr/>		
30 test persons		99.99 %

A comparison between the efficacy of both test compounds in this study shows that compound No. 54 had a sufficient effect on 46.66 per cent of

test persons (16 were free from dandruff or showed dandruff in only physiological quantities), where as test compound No. 56 new had a sufficient effect on only 16.66 per cent of test persons. Fifteen test persons treated with this compound showed a clearly visible dandruff formation, seven test persons showed a medium grade and three test persons even a marked dandruff formation. In my opinion test compound No. 54 is superior to test compound No. 56 new in its anti-dandruff activity.

Signs of intolerance were not observed after treatment with either of the test compounds.

signed:

Prof. Jänner

No. 56 (new) = Seborin shampoo base + 0.2 per cent Zn-Omadine

No. 54 = Seborin shampoo base + 0.5 per cent Octopirox